IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re patent application of:

Grouzmann, *et al.*

Appl. No.: 09/993,959

Filed: November 27, 2001

For: **Method of Treating Rhinitis or Sinusitis**

Art Unit: 1654

Examiner: M. Meller

Atty. Dkt.: 7571/73191
(Formerly 81985/282428)

Amendment and Response Under 37 CFR §1.116

Commissioner of Patents
U.S. Patent and Trademark Office
2011 South Clark Place
Customer Window, **MS AF**
Crystal Plaza Two, Lobby, Room 1B03
Arlington, VA 22202

Sir:

In response to the Office Action dated April 18, 2003, Applicants respectfully reconsideration of the above-captioned application in light of the following remarks.

I. Status of the Application and Claims

The present application was filed as a division of U.S. application 09/794,236 (now U.S. 6,337,069) and had a total of 16 claims. At the time of filing, Applicants submitted a Preliminary Amendment which cancelled claims 1-8, leaving claims 9-16 pending in the application. As the result of a restriction requirement, claim 16 was cancelled and, due to a species election requirement, claims 12, 13 and 14 were withdrawn from consideration. All of the remaining claims, *i.e.*, claims 9-11 and 15, have received a final rejection in the Office Action dated April 18, 2003. For the convenience of the Examiner, all of the rejected claims are repeated in the Appendix of this Response.

II. General Description of the Invention

The present invention is based upon the discovery that the intranasal administration of peptidases that cleave at Xaa-Pro residues, *e.g.*, dipeptidyl peptidase IV, can be used as an

effective treatment to reduce the inflammation associated with respiratory conditions such as rhinitis and sinusitis (see page 2 of the application, lines 23-33). Claims directed to methods of treating patients for mucosal inflammation associated with rhinitis, sinusitis or both were the subject of a previous application that has now issued as U.S. Patent 6,337,069.

In addition, Applicants have disclosed therapeutic packages which contain a device for intranasally delivering drug to a patient and which are preloaded with a solution or powder containing one or more of the peptidases described above (see page 3 of the application, lines 12-14). These devices would allow patients to self-administer drugs by inhalation. It is claims directed to these therapeutic packages that are now under consideration.

III. Issues

All of the claims pending in the above-captioned application have been rejected under 35 U .S.C. § 103 as being unpatentable over four references. The references are: Wilkinson, *et al.* (U.S. 6,251,391); Houston (U.S. 6,447,772); Robison (U.S. 6,395,889); and Petell, *et al.* (U.S. 5,665,595). The Examiner alleges that these references teach the intranasal delivery of dipeptidyl peptidase IV and similar enzymes. Although they do not disclose a preloaded device for intranasally delivering peptidases, it is alleged that making such a device would be obvious.

Applicants believe that, since novelty is not disputed, the relevant issue is whether the references provide an incentive for constructing a preloaded device as claimed. It is Applicants' position that they do not provide such an incentive because: a) prior to the present application, the peptidases were not known to be effective in the treatment of any condition that would make delivery by inhalation a method of choice; b) the references cited are directed to conditions not associated with the respiratory system and expressly state that the preferred method of delivery is oral; and c) intranasal delivery is taught only as one of many alternative non-preferred methods of delivery.

It is important to note that Applicants do not dispute that it was within the capability of those skilled in the art to make preloaded devices and, even without the references, it was

certainly known that drugs could be delivered intranasally. However, it was only after the present application disclosed that peptidases could be used for the treatment of diseases of the respiratory tract that an incentive existed for doing so. Intranasal delivery is a preferred method in the instant application because drug is going directly to the site where inflammation is present. Thus, more would be expected to reach the site where treatment is needed and to do so more rapidly.

IV. Arguments

A. Examiner's Arguments

The Examiner argues that the references cited above teach nasal administration of enzymes that cleave specifically at Xaa-Pro sequences. He therefore concludes that it would be obvious to make a preloaded device for the intranasal delivery of these peptides.

B. Applicants' Response

Response Regarding References by Petell and Robison

Applicants have reviewed the Petell, *et al.*, and Robison references cited in the Office Action and cannot find the exact basis that is being relied upon for rejecting claims. Unless the Examiner can point to specific portions of these references that are relevant to the present allegations, Applicants believe that using them to reject claims is improper.

The Petell reference is concerned with monoclonal antibodies that bind to membrane proteins found on insect cells and to the use of these antibodies for protecting plants from the insects. It bears no clear relationship to the use of peptides as therapeutic agents and does not disclose intranasal delivery.

The Robison reference appears to be based upon a large scale sequencing study in which a variety of protease families were identified using sequence homology data. It is not clear to Applicants whether any of the proteases identified are of the type recited in the present claims. Although intranasal delivery is disclosed as a possible option for delivering proteases, it is included along with a description of essentially every other means of delivering drug. Other options expressly described in the patent include intravenous delivery; intradermal delivery;

subcutaneous delivery; oral delivery (including by means of tablets, pills, capsules, and troches); transdermal delivery; delivery using suppositories and delivery by means of implantable compositions. The patent also suggests that proteases may be delivered by of liposomes or that administration may be accomplished using gene therapy techniques (for a discussion of all of these means of delivery, see col. 57 of the reference, line 41- col. 60, lines 16). There is no suggestion that intranasal delivery is in any way preferred and there is no suggestion that peptidases cleaving specifically at Xaa-Pro sequences might be used in the treatment of a respiratory disease where delivery of drug by inhalation would offer an apparent advantage.

Response Regarding References by Houston and Wilkinson

Neither of the remaining two references, *i.e.*, Houston and Wilkinson, *et al.* suggest that peptidases of the type recited in Applicants' claims might be useful in the treatment of a condition affecting the lungs or respiratory tract. The Houston reference is concerned with the treatment of patients for autism, and the Wilkinson reference is concerned with reducing opioid-related symptoms. Both of the references expressly state that the preferred method of drug delivery is oral (see col. 9, lines 20-21 in the Wilkinson reference, and col. 8, lines 35-36 in the Houston reference). The references then go on to say that essentially any other method of drug delivery can also be used and include intranasal delivery among these. Since the references only teach intranasal delivery as a non-preferred option among many other alternatives and expressly indicate that the preferred method of delivery is oral, they do not provide any incentive for one of skill in the art to make preloaded devices for inhalation containing the peptidases.

Applicants believe that the disclosure of intranasal delivery in the references cited is roughly equivalent to the circumstances considered by the Federal Circuit in *In re Baird* (16 F.3d 380 (Fed. Ed. Cir. 1994)) and summarized in MPEP § 2144.08. Specifically, the references only disclose intranasal delivery as part of a broad genus that includes all methods of administering drugs and they contain no teachings that would lead one of skill in the art to select intranasal delivery from the other options available. Using the teachings of the references, one of skill in the art would be provided with an incentive to prepare a dosage form for oral delivery, *i.e.*, they would have an incentive to make an oral tablet, capsule, or liquid.

C. Conclusion

In light of the discussion above, Applicants submit that the Examiner's rejections have been overcome. It is therefore respectfully requested that these rejections be withdrawn and that the claims presently pending in the application be allowed.

If, in the opinion of the Examiner, a phone call may help to expedite the prosecution of this application, the Examiner is invited to call Applicants' undersigned attorney at (202) 219-7013.

Respectfully submitted,

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